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INTRODUCTION

In this proposal, we hypothesize that inhibition of IGF action by IGFBP-1 will prevent breast cancer in a SV40 Tag transgenic model of breast cancer. We will test this hypothesis with two specific aims: 1) to inhibit IGF action at the mammary epithelial cell by creating transgenic mice that express IGFBP-1 under the control of the whey acidic protein (WAP) promoter and 2) to test the ability of IGFBP-1 to suppress tumorigenesis by mating these animals with C3/Tag transgenic mice.

BODY

Specific Aim (Task) #1 - To inhibit IGF action at the mammary epithelial cell by creating transgenic mice that express IGFBP-1 under the control of the whey acidic protein (WAP) promoter

a. Months 0-3 - Create WAP-IGFBP-1 transgene vector

We have cloned the IGFBP-1 into the appropriate expression vector in animals.

b. Months 3-9 - Create and identify IGFBP-1 F1 progeny

The transgene construct was injected into embryos. Of the 12 animals initially identified, approximately 25% (3 animals) had incorporated the transgene as detected by Southern blot analysis of tail vein DNA. We have spent some time trying to use PCR as a screening method. At this point in time, we are unable to determine the appropriate conditions to use PCR, so we are now relying on Southern blots.

c. Months 9-16 - Characterize level of IGFBP-1 expression in mammary gland, determine influence of IGFBP-1 expression on lactation, examine activation of IGFR1

We have learned the technique of mammary gland dissection (on non-transgenic animals) and have also received advice on the obtaining milk from mice. At present, we are breeding our founders and have not yet analyzed levels of IGFBP-1 protein expression in the milk or mammary gland. We believe that this goal will be accomplished in the next several months.

Specific Aim (Task) #2 - To test the ability of IGFBP-1 to suppress tumorigenesis by mating these animals with C3/Tag transgenic mice

We have not yet begun work on this aim.

KEY RESEARCH ACCOMPLISHMENTS

- ◆ Created the WAP-IGFBP-1 expression construct
- ◆ Generated founder mice with integration of the construct

REPORTABLE OUTCOMES

None.

CONCLUSIONS

We have generated the appropriate construct and now have founder mice. We hope that IGFBP-1 will be expressed at high levels and these animals can be used to test the hypothesis that inhibition of IGF signaling will prevent breast cancer.

REFERENCES

None

APPENDICES

None